

1246 3A 3T3

PRODUCTION OF GP88 BY TUMORIGENIC AND NON-TUMORIGENIC CELLS

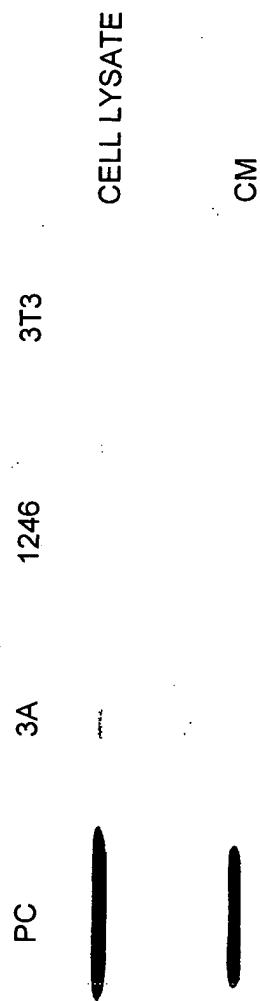


FIG.1A

1 of 30

10000 3400000

GP88 mRNA EXPRESSION

PC 3A 1246 CELLS

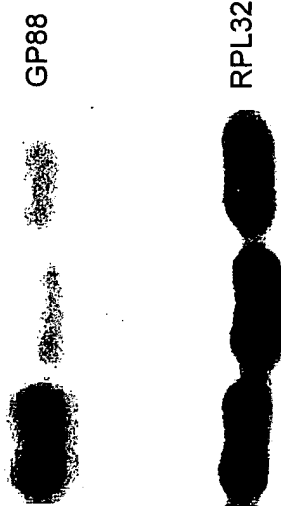


FIG.1B

1246 CELLS

GP88 mRNA EXPRESSION IN VARIOUS CULTURE CONDITIONS

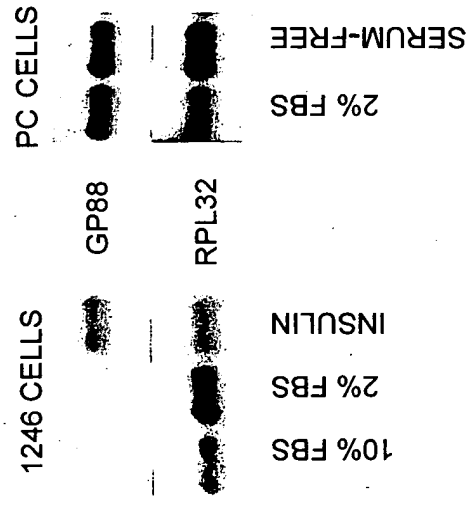


FIG.1C

1000000

1000000

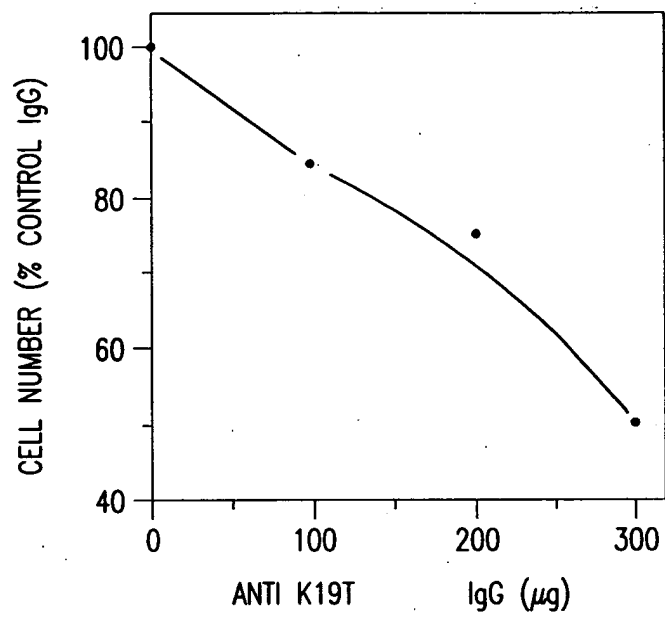
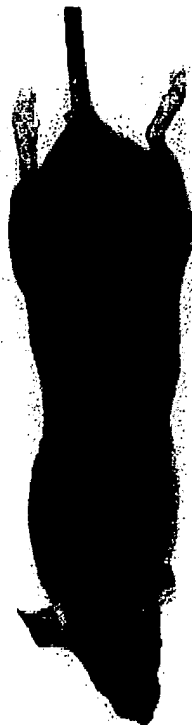


FIG.2

FIG. 3

**ABSENCE OF TUMOR FORMATION IN C3H MICE BY INHIBITION OF GP88
EXPRESSION**



GP88 ANTISENSE TRANSFECTED PC CELLS



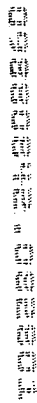
CONTROL TRANSFECTED PC CELLS

FIG.3

[illegible]

FIG. 4

UNCLASSIFIED



GP88 mRNA

UNAP-15MAN

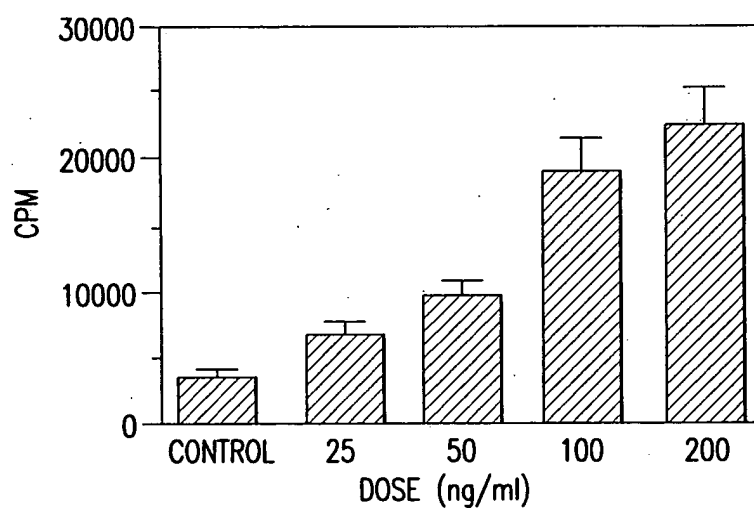


FIG.6A

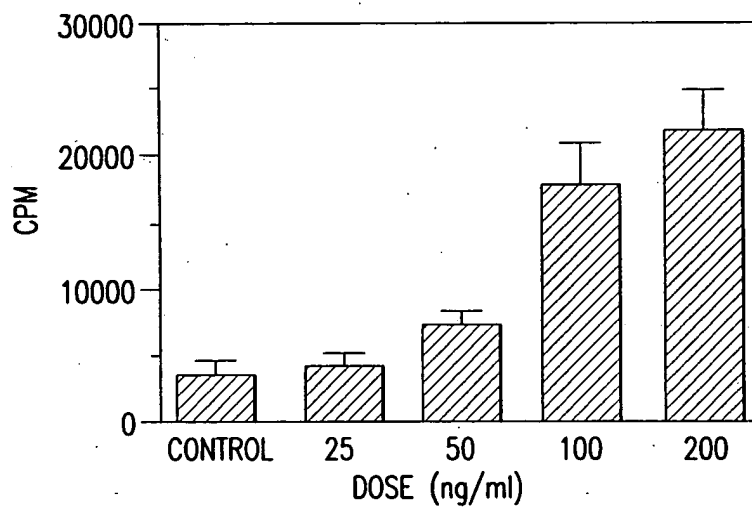


FIG.6B

EXPRESSION OF GP88 IN ANTISENSE AND CONTROL TRANSFECTED PC CELLS

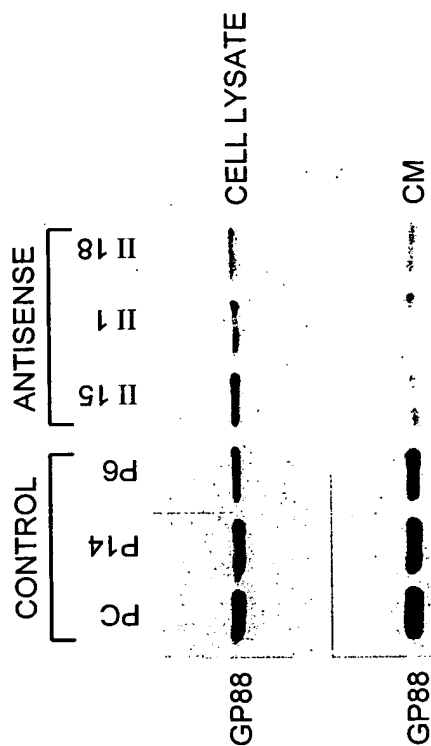


FIG.7

Mouse GP88 cDNA

<p> <u>C</u> GGA CCC CGA CGC AGA CAG ACC ATG TGG GTC CTG ATG AGC TGG CTG M W V L M S W L </p>	<p>46 8</p>
<p> GCC TTC GCG GCA GGG CTG GTA GCC GGA ACA CAG TGT CCA GAT GGG CAG A F A A G L V A G T Q C P D G Q </p>	<p>94 24</p>
<p> TTC TGC CCT GTT GCC TGC TGC CTT GAC CAG GGA GGA GCC AAC TAC AGC F C P V A C C L D Q G G A N Y S </p>	<p>142 40</p>
<p> TGC TGT AAC CCT CTT CTG GAC ACA TGG CCT AGA ATA ACG AGC CAT CAT C C N P L L D T W P R I T S H H </p>	<p>190 56</p>
<p> CTA GAT GGC TCC TGC CAG ACC CAT GGC CAC TGT CCT GCT GGC TAT TCT L D G S C Q T H G H C P A G Y S </p>	<p>238 72</p>
<p> TGT CTT CTC ACT GTG TCT GGG ACT TCC AGC TGC TGC CCG TTC TCT AAG C L L T V S G T S S C C P F S K </p>	<p>286 88</p>
<p> GGT GTG TCT TGT GGT GAT GGC TAC CAC TGC TGC CCC CAG GGC TTC CAC G V S C G D G Y H C C P Q G F H </p>	<p>334 104</p>
<p> TGT AGT GCA GAT GGG AAA TCC TGC TTC CAG ATG TCA GAT AAC CCC TTG C S A D G K S C F Q M S D N P L </p>	<p>382 120</p>
<p> GGT GCT GTC CAG TGT CCT GGG AGC CAG TTT GAA TGT CCT GAC TCT GCC G A V Q C P G S Q F E C P D S A </p>	<p>430 136</p>
<p> ACC TGC TGC ATT ATG GTT GAT GGT TCG TGG GGA TGT TGT CCC ATG CCC T C C I M V D G S W G C C P M P </p>	<p>478 152</p>
<p> CAG GCC TCT TGC TGT GAA GAC AGA GTG CAT TGC TGT CCC CAT GGG GCC Q A S C C E D R V H C C P H G A </p>	<p>526 168</p>
<p> TCC TGT GAC CTG GTT CAC ACA CGA TGC GTT TCA CCC ACG GGC ACC CAC S C D L V H T R C V S P T G T H </p>	<p>574 184</p>
<p> ACC CTA CTA AAG AAG TTC CCT GCA CAA AAG ACC AAC AGG GCA GTG TCT T L L K K F P A Q K T N R A V S </p>	<p>622 200</p>
<p> TTG CCT TTT TCT GTC GTG TGC CCT GAT GCT AAG ACC CAG TGT CCC GAT L P F S V V C P D A K T Q C P D </p>	<p>670 216</p>

FIG.8A

APPROVED	O.G., FIG.	
BY	CLASS	SUBCLASS
DRAFTSMAN		

Mouse GP88 cDNA (continued)

GAT TCT ACC TGC TGT GAG CTA CCC ACT GGG AAG TAT GGC TGC TGT CCA	718
D S T C C E L P T G K Y G C C P	232
ATG CCC AAT GCC ATC TGC TGT TCC GAC CAC CTG CAC TGC TGC CCC CAG	766
M P N A I C C S D H L H C C P Q	248
GAC ACT GTA TGT GAC CTG ATC CAG AGT AAG TGC CTA TCC AAG AAC TAC	814
D T V C D L I Q S K C L S K N Y	264
ACC ACG GAT CTC CTG ACC AAG CTG CCT GGA TAC CCA GTG AAG GAG GTG	862
T T D L L T K L P G Y P V K E V	280
AAG TGC GAC ATG GAG GTG AGC TGC CCT GAA GGA TAT ACC TGC TGC CGC	910
K C D M E V S C P E G Y T C C R	296
CTC AAC ACT GGG GCC TGG GGC TGC TGT CCA TTT GCC AAG GCC GTG TGT	958
L N T G A W G C C P F A K A V C	312
TGT GAG GAT CAC ATT CAT TGC TGC CCG GCA GGG TTT CAG TGT CAC ACA	1006
C E D H I H C C P A G F Q C H T	328
GAG AAA GGA ACC TGC GAA ATG GGT ATC CTC CAA GTA CCC TGG ATG AAG	1054
E K G T C E X G I L Q V P W M <u>K</u>	344
AAG GTC ATA GCC CCC CTC CGC CTG CCA GAC CCA CAG ATC TTG AAG AGT	1102
<u>K V I A P L R L P D P Q I L K S</u>	360
GAT ACA CCT TGT GAT GAC TTC ACT AGG TGT CCT ACA AAC AAT ACC TGC	1150
<u>D T</u> P C D D F T R C P T N N T C	376
TGC AAA CTC AAT TCT GGG GAC TGG GGC TGC TGT CCC ATC CCA GAG GCT	1198
C K L N S G D W G C C P I P E A	392
GTC TGC TGC TCA GAC AAC CAG CAT TGC TGC CCT CAG GGC TTC ACA TGT	1246
V C C S D N Q H C C P Q G F T C	408
CTG GCT CAG GGG TAC TGT CAG AAG GGA GAC ACA ATG GTG GCT GGC CTG	1294
L A Q G Y C Q K G D T M V A G L	424
GAG AAG ATA CCT GCC CGC CAG ACA ACC CCG CTC CAA ATT GGA GAT ATC	1342
E K I P A R Q T T P L Q I G D I	440

FIG.8B

APPROVED	O.G. FIG.	
BY	CLASS	SUBCLASS
DRAFTSMAN		

Mouse GP88 cDNA (continued)

GGT TGT GAC CAG CAT ACC AGC TGC CCA GTA GGG CAA ACC TGC TGC CCA	1390
G C D Q H T S C P V G Q T C C P	456
AGC CTC AAG GGA AGT TGG GCC TGC TGC CAG CTG CCC CAT GCT GTG TGC	1438
S L K G S W A C C Q L P H A V C	472
TGT GAG GAC CGG CAG CAC TGT TGC CCG GCC GGG TAC ACC TGC AAC GTG	1486
C E D R Q H C C P A G Y T C N V	488
AAG GCG AGG ACC TGT GAG AAG GAT GTC GAT TTT ATC CAG CCT CCC GTG	1534
K A R T C E K D V D F I Q P P V	504
CTC CTG ACC CTC GGC CCT AAG GTT GGG AAT GTG GAG TGT GGA GAA GGG	1582
L L T L G P K V G N V E C G E G	520
CAT TTC TGC CAT GAT AAC CAG ACC TGT TGT AAA GAC AGT GCA GGA GTC	1630
H F C H D N Q T C C K D S A G V	536
TGG GCC TGC TGT CCC TAC CTA AAG GGT GTC TGC TGT AGA GAT GGA CGT	1678
W A C C P Y L K G V C C R D G R	552
CAC TGT TGC CCC GGT GGC TTC CAC TGT TCA GCC AGG GGA ACC AAG TGT	1726
H C C P G G F H C <u>S A R G T K C</u>	568
TTG CGA AAG AAG ATT CCT CGC TGG GAC ATG TTT TTG AGG GAT CCG GTC	1774
<u>L R K K I P R</u> W D M F L R D P V	584
CCA ACA CCG CTA CTG TAA GGA AGG GCT ACA GAC TTA AGG AAC TCC ACA	1822
P R P L L *	589
GTC CTG GGA ACC CTG TTC CGA GGG TAC CCA CTA CTC AGG CCT CCC TAG	1870
CGC CTC CTC CCC TAA CGT CTC CCC GGC CTA CTC ATC CTG AGT CAC CCT	1918
ATC ACC ATG GGA GGT GGA GCC TCA AAC TAA AAC CTT CTT TTA TGG AAA	1966
GAA GGC TGT GGC CAA AAG CCC CGT ATC AAA CTG CCA TTT CTT CCG GTT	2014
TCT GTG GAC CTT GTG GCC AGG TGC TCT TCC CGA GCC ACA GGT GTT CTG	2062
TGA GCT TGC TTG TGT GTG TGT GCG CGT GTG CGT GTG TTG CTC <u>QAA TAA</u>	2110
<u>AGT</u> TTG TAC GCT TTC TGA AAA AAA AAA	2137

FIG.8C

Nucleotide sequence of human granulin/epithelin precursor (human GP88).
Human Granulin Genbank M75161\$

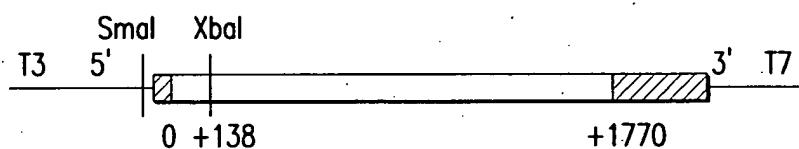
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gccagctaca gctgctgccg tccccctctg gacaaatggc ccacaacact gagcaggcat
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ccacaagcct tgaagagaga tgtccctgt gataatgtca gcagctgtcc ctctccgat
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tgctcggacc accagactg ctgccccag cgatacacgt gtgtagctga ggggcagtgt
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gatcgccagc actgctgccc ggctggctac acctgcaacg tgaaggctcg atcctgcgag
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aaccgacagg gctgggcctg ctgtccctac gccaggggcg tctgttgtgc tgatcggcgc
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gtactgaaga ctctgcagcc ctgaggacc cactcggagg gtgcctctg ctcaggcctc
gtactgaaga ctctgcagcc ctgaggacc cactcggagg gtgcctctg ctcaggcctc
cctagcact cccctaacc aaattctccc tggaccccat tctgagctcc ccatcaccat
gggaggtggg gcctcaatct aaggcccttc cctgtcagaa gggggttag gcaaaagccc
attacaagct gccatccct cccggtttca gtggaccctg tggccagggt cttttcccta
tccacagggg tgtttgtgtg ttgggtgtgc tttaataaa gtttgcact ttctt*

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FIG.9A

GP88 cDNA CLONE in SK



STRUCTURE OF pCMV₄ EXPRESSION VECTOR

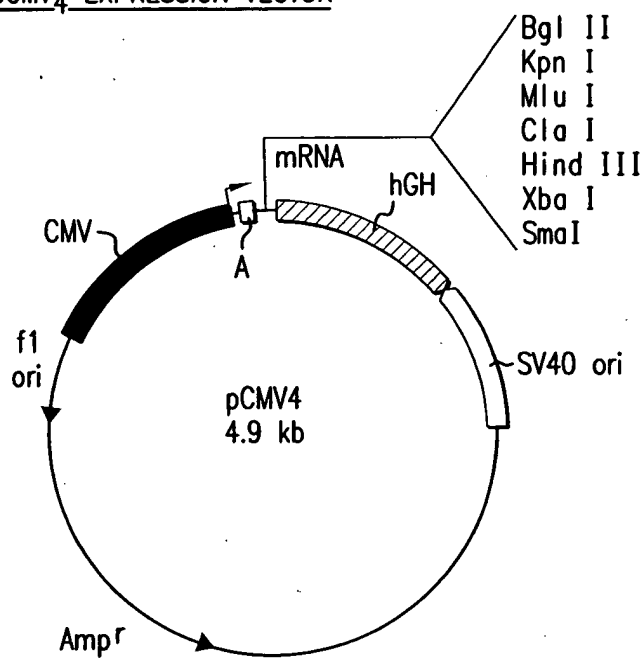


FIG.11

**GP88 EXPRESSION IN NON TUMORIGENIC (MCF 10A)
AND MALIGNANT (MCF 7, MDA-468) HUMAN
MAMMARY EPITHELIAL CELLS**

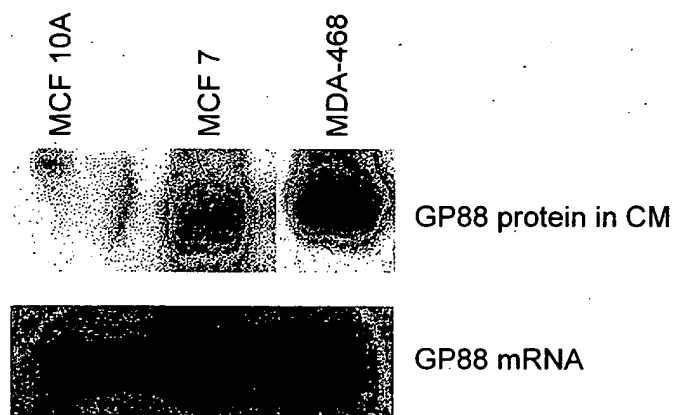


FIG.14

**GP88 EXPRESSION IS INHIBITED BY ANTISENSE GP88
cDNA TRANSFECTION IN HUMAN BREAST
CARCINOMA MDA-468**

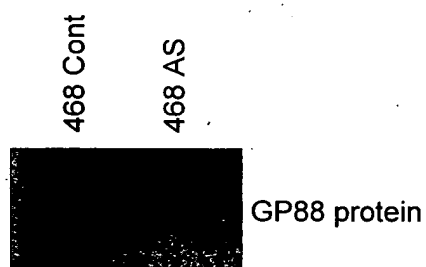


FIG.15

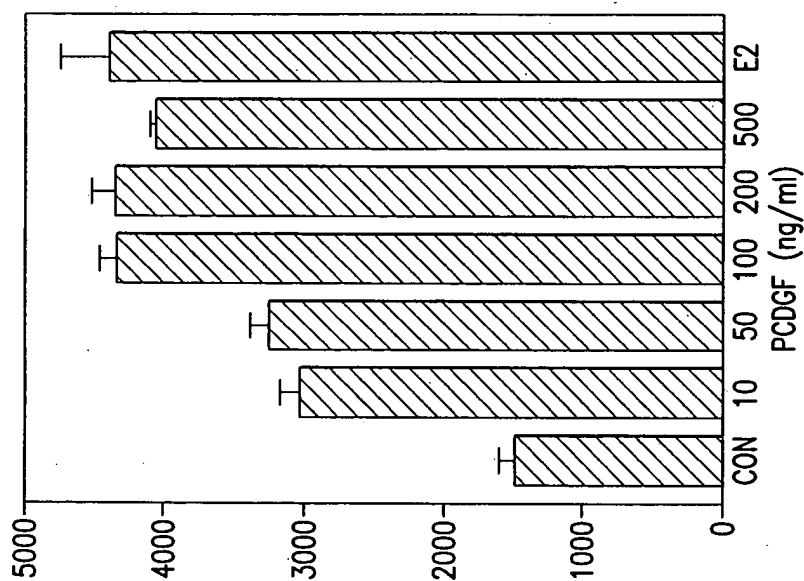


FIG.16A

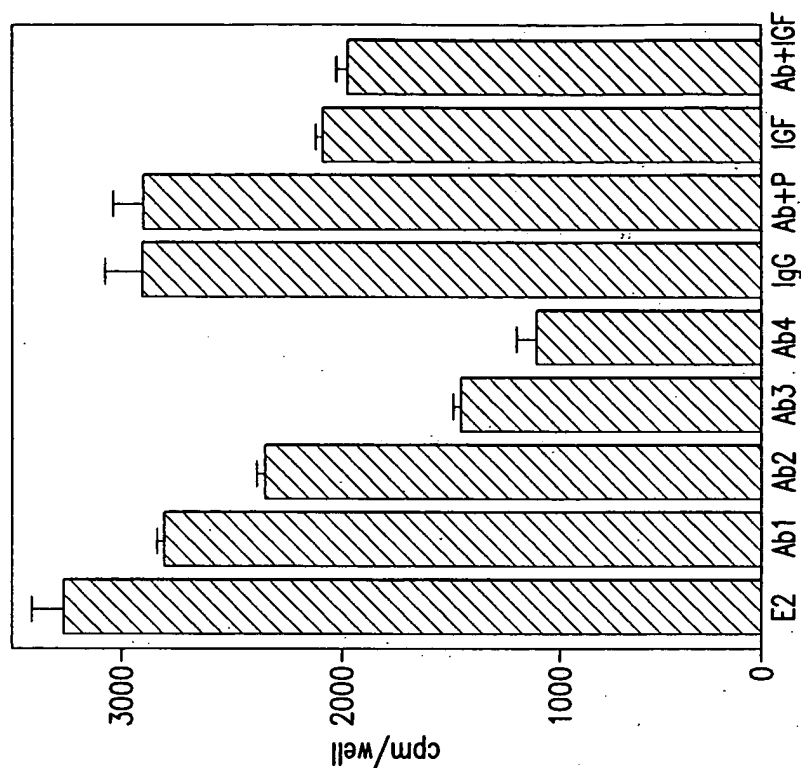


FIG.16B

AS13

AS22

C



FIG.17A

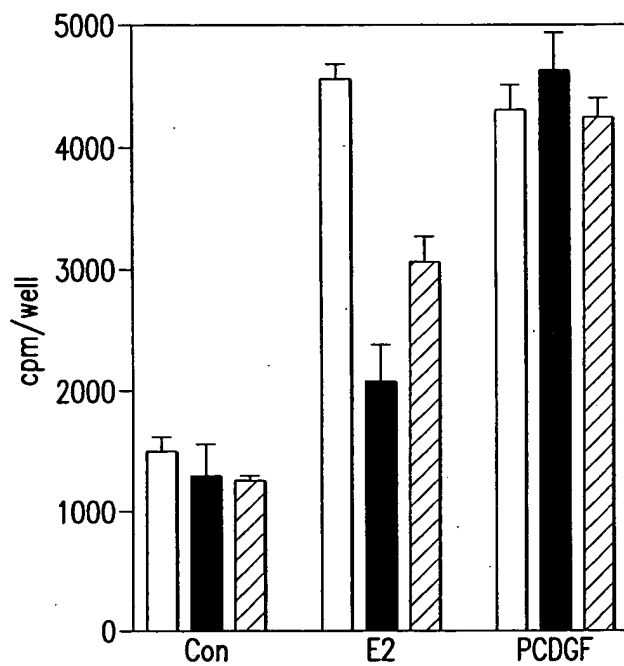


FIG.17B

FIG. 18A

FIG. 18B

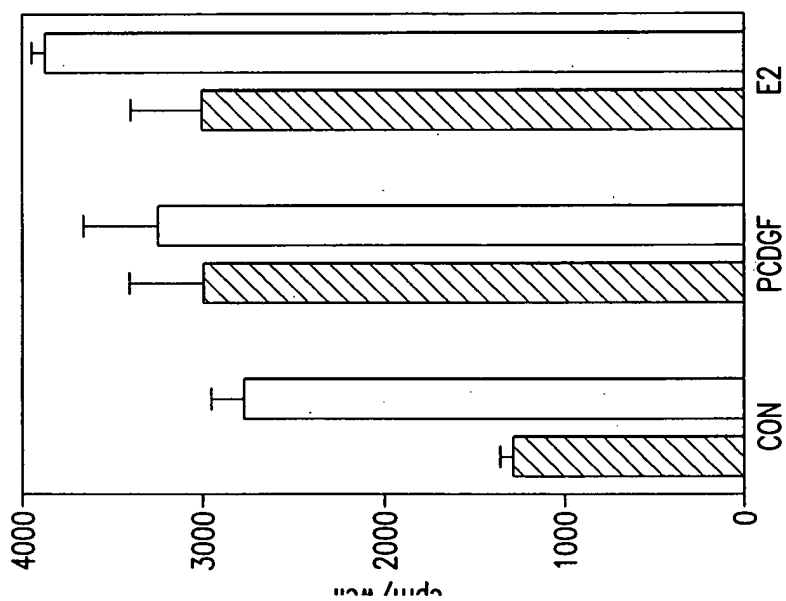


FIG.18B

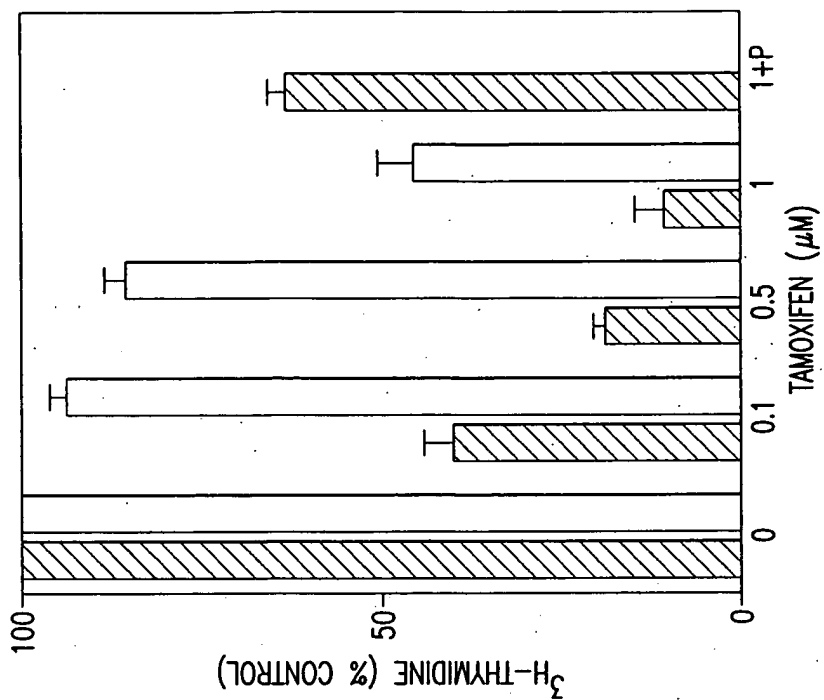


FIG.18C

APPROVED	O.G. FIG.	
BY	CLASS	SUBCLASS
DRAFTSMAN		

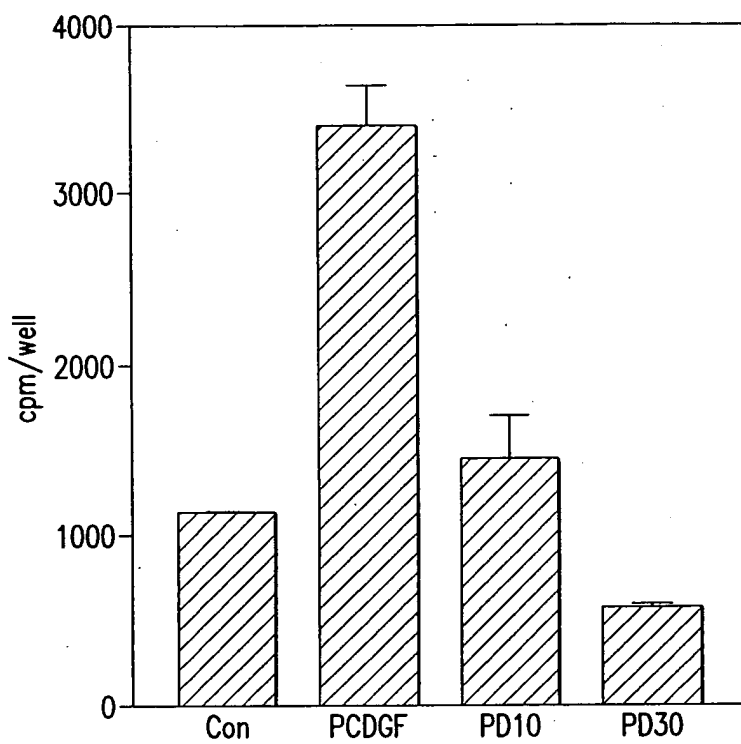


FIG.19A

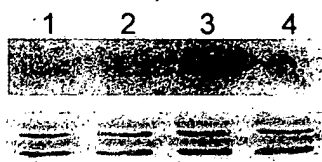


FIG. 19B

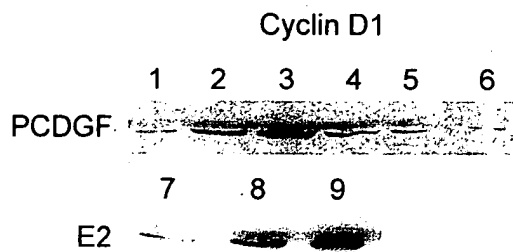


FIG.20A

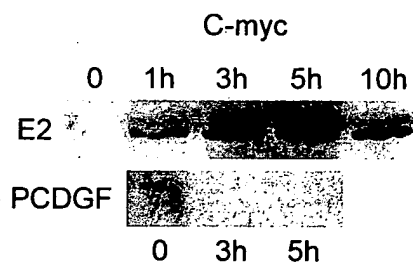


FIG.20B

FIG. 23

TAMOXIFEN RESPONSIVENESS OF ER+ IDC TUMORS CLASSIFIED
BY GP88 STAINING INTENSITY

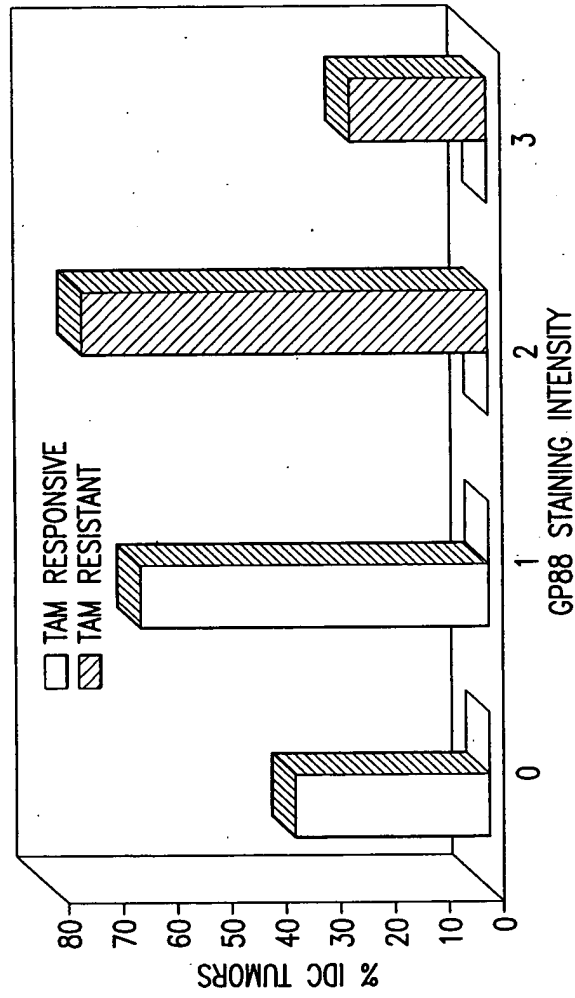


FIG. 23



BENIGN LESION



DUCTAL INVASIVE CARCINOMA

GP88 STAINING WITH ANTI-GP88 ANTIBODY
ON PARAFFIN EMBEDDED BREAST CANCER BIOPSIES
BY IMMUNOHISTOCHEMISTRY (IHC)

FIG.21

APPROVED	O.G. FIG.	
BY	CLASS	SUBCLASS
DRAFTSMAN		

FIG. 22

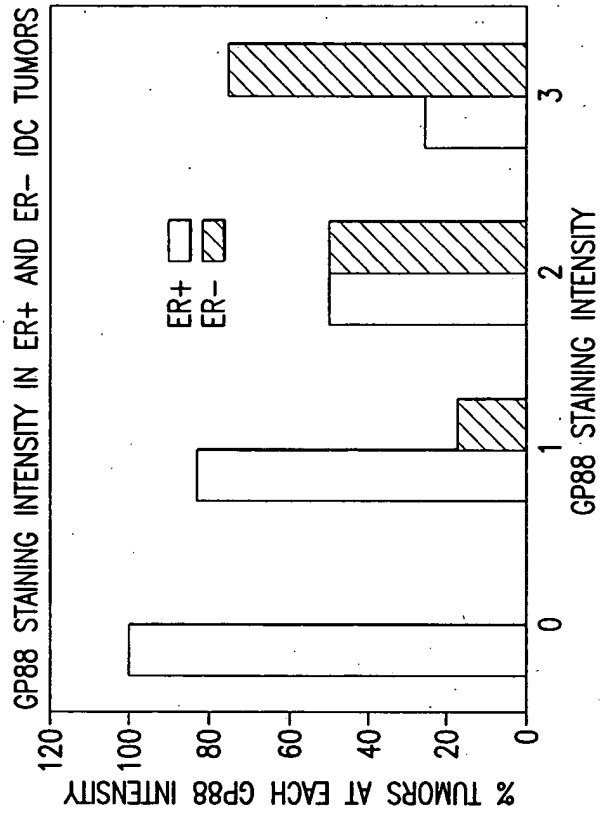


FIG.22